REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

The title has been replaced with a new title in accordance with the suggestion of the Examiner. Accordingly, this ground of objection is deemed to be overcome.

Claim 20 has been revised to correct the informality noted in the action.

Accordingly, this ground of objection is deemed to be overcome.

Claims 1-20 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite based upon the phrase "aldehyde-like". This phrase is defined on page 7, line 22 to page 8, line 18 of the specification. The claims have been amended accordingly.

In view of the foregoing, this ground of rejection is deemed to be overcome.

Other amendments to the claims are noted as follows.

The claims have been amended to specify the stabilizer, according to the definition set forth in claim 3. Accordingly, claims 2 and 3 have been deleted without prejudice.

The claims have been revised to clarify that each claimed composition is a pharmaceutical composition such as recited in original claim 11.

In claim 4, "gelatin" has been deleted since this member has been excluded from the definition of the stabilizer.

Turning to the substantive grounds of rejection, claims 1-10 were rejected under 35 U.S.C. 102 as anticipated by Bunczek et al. (US Patent 5,192,561). Claims 16 and 17 were also rejected under 35 U.S.C. 102 as anticipated by Bunczek et al. These grounds of rejection are deemed to be overcome as applied to the amended claims.

The Claimed Invention

The present invention provides a stabilized pharmaceutical composition containing a low-molecular weight active substance the stability of which is impaired by the effects of aldehydes and a specific substance being capable of supplying aldehyde-like substances as specified in the amended claim 1. The stabilization of the active substance is effected by incorporating a specific

stabilizer as defined in the amended claim 1. There is further provided a method for the stabilization of the active substance with said specific stabilizer.

Thus, the pharmaceutical composition of the present invention contains a substance being capable of supplying aldehyde-like substances which is, as defined in the present disclosure, page 7, line 22 to page 8, line 4, a substance having an aldehyde structure or a substance being capable of producing or generating a compound having an aldehyde structure during the production process of the composition or during storage of the composition by interaction with other components in said composition or with environmental factors (e.g., moisture, oxygen, carbon dioxide). Specific examples of said substance are mentioned in the present disclosure, page 8, lines 6-18. In the amended claims, this substance is specified by these specific examples as mentioned above.

The present invention is characteristic in that the possible impairment of the active substance in the composition due to the substance being capable of supplying aldehyde-like substances is prevented/inhibited by incorporation of a specific stabilizer having an amine structure and being capable of absorbing aldehydes.

Said specific stabilizer is explained in the present disclosure, page 10, line 12 to page 11, line 8, and is defined in the original claim 3. Now, the stabilizer is specified in amended claim 1 as well as other claims, while gelatin or a hydrolysate thereof was excluded in order to distinguish more clearly from the cited Bunczek et al. reference.

With respect to the low-molecular weight active substance, the active substance is well explained in the present disclosure, page 8, line 19 to page 9, line 6, and the exemplified active substances have a molecular weight of about 150 to about 400.

The Cited Reference

The invention of Bunczek et al. is concerned with a method for stabilizing aspartame, when aspartame is used in chewing gum along with aldehyde type flavors. That is, the aspartame is used as a sweetener for chewing gum and its stability is impaired by the co-existent aldehyde type flavoring agents, particularly cinnamic aldehyde (of cinnamon flavor), and then the aspartame is stabilized by mixing with an encapsulating agent and an acid.

It is mentioned in Bunczek et al. at col. 3, lines 13-22 as follows:

"Next, an encapsulating agent, preferably gelatin, is added to the solution of APM, water and acid, in order to thicken the solution. Alternative encapsulating agents include those that are water soluble like agar, alginates, a wide range of cellulose derivatives like ethyl cellulose, methyl cellulose; sodium hydroxymethyl cellulose and hydroxypropylmethyl cellulose, dextrins, maltodextrins, modified starches, and vegetable gums like guar gum, locust bean gum, carageenin gum and gum acacia."

In Bunczek et al., the encapsulating agent to be used for stabilizing aspartame includes a gelatin as a preferred one, and further includes various kinds of substance, such as those water soluble like agar, alginates, a wide range of cellulose derivatives like ethyl cellulose, etc. dextrins, maltodextrins, modified starches and vegetable gums like guar gum, etc.

As mentioned above, gelatin was excluded from the stabilizer in claim 1 and the other claims of the present invention, and the other encapsulating agents disclosed in Bunczek et al. do not have an amine structure. Hence they are clearly distinguished from the stabilizer of the present invention.

Thus, Bunczek et al. discloses merely stabilizing aspartame in chewing gum by mixing an encapsulating agent (preferably gelatin) and an acid, but does never teach or even suggest the characteristic feature of the present invention, that is, stabilizing a low-molecular weight active substance the stability of which is impaired by the effects of aldehydes produced or generated by coexistence of a specific substance being capable of supplying aldehyde-like substances. In the present invention, the stabilization of the active substance is effected by incorporating a specific stabilizer as defined in the amended claim 1, which is clearly distinguished from the encapsulating agent of Bunczek et al.

Accordingly, the claimed invention as amended is not taught, or even suggested, by Bunczek et al.

Claims 1-10 were rejected under 35 U.S.C. 102 as anticipated by Nomura et al. (WO/01/74397). Claims 1, 16 and 7 were also rejected under 35 U.S.C. 102 as anticipated by

Nomura. These grounds of rejection are deemed to be overcome as applied to the amended claims.

The Cited Reference

It is disclosed in Nomura et al that "The present invention relates to a powdery preparation for transmucosal administration comprising a medicine of high molecular weight and a cationic polymer, the preparation further comprising a basic amino acid and exhibiting an improved storage stability. Particularly, the invention relates to such a preparation for administration through the nasal mucosa." (cf. US 2005/0037084A1, page 1, paragraph [0001])

Besides, the basic amino acid to be used in Nomura et al. includes L-arginine (cf. US 2005/0037084A1, page 2, paragraph [0025]) and further the excipient used in Nomura et al. Includes mannitol, starch (cf. US 2005/0037084A1, page 3, paragraph [0027]).

However, the medicine of Nomura et al. is a high molecular weight substance, although it is mentioned that the medicine may include a low molecular weight compound in US 2005/0037084A1, page 2, paragraph [0021] after listing various medicines as follows:

"It can be readily estimated that even with medicines with smaller molecular weight than the above examples of the medicine of high molecular weight, the present invention can increase their absorption through mucous membranes, particularly nasal mucosa, and therefore the present invention is believed also useful in applications with a medicine of low-molecular weight."

Nevertheless, in the Nomura working examples, there is used only G-CSF which has a molecular weight of 20kDa, which molecular weight is much higher than the low molecular weight of the active substance in the present invention. And there is no specific disclosure of a low molecular weight medicine in any working example of Nomura et al.

Moreover, it shall also be noted that the wording "and therefore the present invention is believed also useful in applications with a medicine of low-molecular weight" in the above paragraph [0021] was added when entering into the national phase in the U.S.A. Thus, this wording is not found in the cited WO 01/74397. Hence the stability of a low molecular weight medicine has never been disclosed or even suggested before the priority date (even before the filing date) of the present application.

Accordingly, the present invention as claimed in claims 1-10, 11, 16 and 17 is not anticipated by Nomura et al.

With respect to claim 20, which is not encompassed by the rejections, the Examiner points out that Nomura et al. teaches preparing a solution/mass comprising mannitol and L-arginine and a solution/mass comprising a low molecular weight ([0021]) active substance ([0048]).

However, as mentioned above, Nomura et al. teach merely stabilization of a high molecular weight medicine, and further Nomura et al. do not teach or even suggest to incorporate the specific stabilizer as used in the present invention in order to prevent or inhibit the impairment of the medicine by aldehydes.

Accordingly, the present invention as claimed in claim 20 is clearly distinguished from the cited Nomura et al. reference.

Claims 12-15 are rejected under 35 U.S.C. 103 as unpatentable over Nomura et al. in view of Kurihara et al. (US Patent 5,726,180). Claims 18 and 19 are also rejected under 35 U.S.C. 103 as being unpatentable over Nomura et al. and Kurihara et al. These grounds of rejection are deemed to be overcome in view of the amended claims.

The Cited References

As is explained above, Nomura et al. do not disclose or even suggest the characteristic feature of the present invention, that is, the stabilization of the low-molecular weight active substance the stability of which is impaired by the effects of aldehydes by inhibiting the effects of aldehydes with a specific stabilizer having an amine structure and being capable of absorbing aldehydes.

As pointed out by the Examiner, Kurihara et al discloses "forming fine granules of the ingredients of a drug composition where the ingredients are separated". However, Kurihara et al do not teach or even suggest the characteristic feature of the present invention of the stabilization of the low-molecular weight active substance the stability of which is impaired by the effects of aldehydes by inhibiting the impairing effects of aldehydes with a specific stabilizer having an amine structure and being capable of absorbing aldehydes.

Accordingly, even by combining the teachings of the primary Nomura et al. reference with the secondary Kurihara et al. reference, the present invention as claimed in claims 12-15 and claims 18 and 19 having the above mentioned characteristic feature would have never been predicted from these references and is patentable over the cited references.

In view of the foregoing, it is believed that each ground of rejection set forth in the Official Action has been overcome and that the application is in condition for allowance. Accordingly, such allowance is listed.

Regarding the Examiner's request for information about common ownership of the claimed invention, please be advised that the subject matter as claimed in each claim has been commonly owned by the inventors when the invention was made as listed in the following table.

Claims	Inventors	Date of Invention
1 to 10	Motokazu Iwata Megumi Fujita Hideo Kurita	October 22, 2002
11 to 20	Motokazu Iwata Megumi Fujita Hideo Kurita Kenichiro Kiyoshima	June 30, 2003

Favorable action and allowance is solicited.

Respectfully submitted,

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